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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,693	01/19/2001	Daniel S. Sem	P-TB 4568	6461

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EXAMINER
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BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 05/19/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/765,693</b>	Applicant(s) <b>Sem</b>						
	Examiner <b>Maurie G. Baker, Ph.D.</b>	Art Unit <b>1639</b>						
<b>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</b>								
<b>Period for Reply</b> <p>A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>THREE</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.</p> <ul style="list-style-type: none"> <li>- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.</li> <li>- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.</li> <li>- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.</li> <li>- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).</li> <li>- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).</li> </ul>								
<b>Status</b> <p>1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Feb 12, 2003</u></p> <p>2a) <input checked="" type="checkbox"/> This action is FINAL.      2b) <input type="checkbox"/> This action is non-final.</p> <p>3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i>, 1935 C.D. 11; 453 O.G. 213.</p>								
<b>Disposition of Claims</b> <p>4) <input checked="" type="checkbox"/> Claim(s) <u>15-19 and 37-61</u> is/are pending in the application.</p> <p>4a) Of the above, claim(s) <u>15-19, 37-41, and 57-61</u> is/are withdrawn from consideration.</p> <p>5) <input type="checkbox"/> Claim(s) _____ is/are allowed.</p> <p>6) <input checked="" type="checkbox"/> Claim(s) <u>42-56</u> is/are rejected.</p> <p>7) <input type="checkbox"/> Claim(s) _____ is/are objected to.</p> <p>8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.</p>								
<b>Application Papers</b> <p>9) <input type="checkbox"/> The specification is objected to by the Examiner.</p> <p>10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).</p> <p>11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.</p> <p>12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.</p>								
<b>Priority under 35 U.S.C. §§ 119 and 120</b> <p>13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</p> <p>*See the attached detailed Office action for a list of the certified copies not received.</p>								
<p>14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.</p> <p>15) <input checked="" type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.</p>								
<b>Attachment(s)</b> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">1) <input type="checkbox"/> Notice of References Cited (PTO-892)</td> <td style="width: 50%;">4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____</td> </tr> <tr> <td>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</td> <td>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</td> </tr> <tr> <td>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____</td> <td>6) <input type="checkbox"/> Other: _____</td> </tr> </table>			1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____	2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)	3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____	6) <input type="checkbox"/> Other: _____
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3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____	6) <input type="checkbox"/> Other: _____							

## DETAILED ACTION

1. The Response filed February 12, 2003 (Paper No. 15) is acknowledged. Claims 42-61 were added and no claims were cancelled or amended in this response. Therefore, claims 15-19 and 37-61 are pending.
2. Applicant has submitted new claims 42-61. Some of these claims are deemed to read on the previously examined invention and thus the case has been further examined on the merits as it now contains claims to the elected invention. However, the examiner maintains that amended claims 15-19 and newly filed claims 37-41 (from the amendment filed on September 25, 2002) are drawn to a different invention than the one currently under examination with respect to the new limitation that the common ligands are compounds that compete for cofactor binding. The same is true for claims 57-61 that are newly added in the Response filed February 12, 2003. Thus, claims 15-19, 37-41 and 57-61 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons.
3. As stated in the Communication mailed 3/27/2002, the claims previously under examination recited a "common ligand to a conserved site in a receptor family". There was **nothing** present in the previously examined claims with respect to competitive binding. Thus claims 15-19, 37-41 and newly filed claims 57-61 are different in scope and represent an invention that is independent or distinct from the invention originally claimed.

4. Also as stated by the examiner previously, the limitation of “wherein said common ligand competes for cofactor binding” would require a completely different search due to different classification and/or divergent subject matter of such a “common ligand” and there is no expectation that the searches would be coextensive. Furthermore, art anticipating or rendering obvious a “common ligand to a conserved site in a receptor family” would not necessarily anticipate or render obvious a common ligand that *competes* for cofactor binding, because they are drawn to different inventions that have different distinguishing features and/or characteristics. See also paragraph 7 below.

5. Applicants traverse the examiner’s position with respect to the above matter in the Response filed February 12, 2003. The examiner did not find the traversal persuasive for the following reasons. First, when one looks to the instant specification, one can see that the definition of “common ligand” (page 8, lines 29-31) is as follows: “the term “common ligand” refers to a ligand that binds to a conserved site in a receptor family”. The original claims recited a “common ligand to a conserved site in a receptor family”. The definition in the instant specification for “conserved site” is “the amino acid residues sufficient for activity or function of the receptor that are accessible to binding of a natural common ligand” (page 13, lines 24-27). As stated in the Response filed February 12, 2003, a “natural common ligand” is a cofactor. Thus, the examiner’s position is that the originally claimed “common ligand to a conserved site in a receptor family” would read on a common ligand that is a cofactor (or mimic) thereof and/or a common ligand that

binds in the cofactor binding site and would not necessarily include common ligands “wherein said common ligand competes for cofactor binding”.

6. Second, “wherein said common ligand competes for cofactor binding” is a process limitation. It is recognized that the claimed invention is itself a process, but it is a process of “identifying” a product (bi-target ligand) made up of three parts: a “common ligand” a “first specificity ligand” and a “second specificity ligand” (as originally claimed). The addition of the limitation “wherein said common ligand competes for cofactor binding” adds a process limitation to the claimed invention that was *not previously there*. Applicant states that “the specification teaches that competing for cofactor binding is in fact a method for identifying a common ligand”. However, the originally examined claims contained nothing with respect to limitations on identifying a common ligand *per se*. The claims were drawn to a “method for identifying a bi-target ligand to a receptor”. There was not a step in the previously examined method that requires identifying a common ligand by using a process of competing for cofactor binding.

7. Third, applicant argues that the limitation “wherein said common ligand competes for cofactor binding” would not require a separate search. The examiner respectfully disagrees. One could easily envision art that would read on a common ligand that is a cofactor or mimic thereof and/or a common ligand that binds in the cofactor binding site that would not read on a common ligand “wherein said common ligand competes for

cofactor binding". The original search of the limitation "common ligand to a conserved site in a receptor family" would not be expected to be coextensive with the added limitation of "wherein said common ligand competes for cofactor binding".

8. Thus, since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 15-19, 37-41 and newly filed claims 57-61 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Restriction for examination purposes as indicated is proper and is made FINAL.

9. Therefore, claims 42-56 are examined on the merits in this action.

*Status of Rejections*

10. All previous rejections are maintained. However, some rewording of the rejections has been made in light of applicant's claim amendments and addition of new claims (thus the changes to the rejections were necessitated by applicant's amendments). Applicant's arguments that were presented in the Response filed September 25, 2002 are addressed following each rejection.

*Maintained Rejections*  
*Claim Rejections - 35 USC § 112*

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 42-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a "method for identifying a bi-target ligand to enzymes in an enzyme family". The identified "bi-target ligand" is made up of three parts: a "common ligand", a "second ligand" and a "third ligand". The claims use generic terminology such as "cofactor binding site", "cofactor or mimic thereof", "second ligand", "third ligand", "substrate binding site", "enzyme family" and "linker". These terms are defined/discussed in the instant disclosure but the definitions are very broad and open-ended.

No specific structure of the identified "bi-target ligand" is set forth and no specific "method for identifying a bi-target ligand" is described in the instant disclosure. The present application fails to describe a specific example of identifying even a single compound which is within the scope of the presently claimed invention. Applicant's claimed scope represents only an invitation to

experiment regarding possible identified “bi-target ligands” within the scope of the claims.

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by “representative examples”) for both enablement and adequate disclosure.

Again, the specification discloses **no** examples of the preparation and use of such “bi-target ligands”. These compounds (i.e. “common ligand”)/“cofactor or mimic thereof”, “second/third ligand[s]” and “linker”) could encompass very different moieties of widely varying structures. Thus, the disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which

are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

***Response to Arguments***

13. Applicant's arguments filed September 25, 2002 have been fully considered but are not found persuasive. It is noted for the record that applicant's arguments in this response are directed at the previously examined claims 15-19 (from the first Office Action on the merits). These claims have since been amended and are now withdrawn from consideration (see paragraphs 2-8 above). As newly added claims 42-56 are deemed to read on the previously examined invention, they are examined in this action and the arguments are addressed in as much as they pertain to rejection of these claims. The examiner's rationale is set forth below.

14. It is recognized that the claims have been amended to state that the receptor is an "enzyme in an enzyme family" and that (1) the common ligand is a "cofactor or mimic thereof" (claim 42 and dependent claims); (2) the common ligand is a "cofactor or mimic thereof" and the "enzyme family comprises two or more enzymes that bind the same cofactor" (claim 47 and dependent claims); or (3) the common ligand "binds to a cofactor binding site" (claim 52 and dependent claims). However, the claims are still deemed to lack adequate description. The addition of the above phrases adds little to overcome the description deficiencies. The situation remains that (as stated in the rejection) *no specific structure* of the identified "bi-target ligand" compounds is set forth. Again, the present

application fails to describe a specific example of even a single compound which is identified utilizing the presently claimed method. Applicant's claimed scope represents only an invitation to experiment regarding possible identified "bi-target ligand" compounds.

15. Applicant argues that the claims are adequately described, citing portions of the specification for support (Response, pages 6-8). The examiner's maintains that the definitions in the specification for the terms discussed in the rejection are *very broad* and *open-ended*. The instant claims give ***no structure*** for the entities that make up the identified "bi-target ligands" ("common ligand"/"cofactor or mimic thereof", "second/third ligand[s]" and "linker") and no structural information as to how they are to be linked together to form such "bi-target ligands". Thus the claims could encompass an infinite number of variations. Note that "the essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978). Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822).

16. The language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in

terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

17. Also, the rejection sets forth the need for representative examples in an unpredictable art that are necessary to demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure); all cited above. The more unpredictable the art the greater the showing required (e.g. by “representative examples”) for both enablement and adequate disclosure. Again, no working examples whatsoever have been provided in the instant case. Applicant argues that examples are provided (Response, page 8); however, applicant is referring to general teachings and prophetic statements.

18. Applicant also argues that the “specification further teaches that methods such as NMR can be applied to identify sites of a common ligand proximal to a specificity site” and other methodology for orientation and linking of ligands (Response, page 8). However, this bears little correlation to the steps of the instantly claimed method and the

portions of the specification referred to are prophetic and general in nature. Again, the specification does not describe any specific "bi-target ligands" that are identified or any specific "method for identifying a bi-target ligand".

19. Lastly, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). The examiner maintains because of the breadth of the claims, the unpredictability of the art and the lack of any working examples, the above standard is not met. Thus the above rejection under 35 U.S.C. 112, first paragraph is maintained.

20. Claims 42-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;

- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a “method for identifying a bi-target ligand” where the “bi-target ligand” is made up of three parts: a “common ligand”, a “second ligand” and a “third ligand”. No limitations on the specific structure of the identified “bi-target ligand” are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the “common ligand” and “second/third ligands” must bind to their respective sites and the sites must be able to be determined. The state of the prior art and the level of predictability in the art: Compounds that interact with various enzyme targets were known in the art at the time of filing; however, only limited numbers of such compounds were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* such compound. The identified “bi-target ligands” of the instant claims require “common ligands” and “second/third ligands”; however, such trimeric ligands for enzyme families were not generally known in the art. The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict their structures. Moreover, the claims require the presence of a “common ligand” which binds to a “cofactor site” or is

a “cofactor or mimic thereof” and two additional ligands that bind to “substrate binding sites” of a first and a second enzyme in an “enzyme family”. One of ordinary skill would not know, *a priori*, how to determine the structure of such ligands because the determination of the different binding sites in an “enzyme family” would be unpredictable. Applicant’s claimed scope of compounds represents only an invitation to experiment regarding possible methods of identification of undefined “bi-target ligands” (see also above rejection concerning written description and cases cited therein). The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. The existence of working examples and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: Applicants have provided **no** working examples and the state of the prior art is such that one of ordinary skill could not predict how to determine and then link the various moieties that make up the identified “bi-target ligand” as required by the instant claims. Therefore, further research would be necessary to make or use the invention and it would require undue experimentation to carry out the invention as claimed. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is

deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the invention would require undue experimentation.

***Response to Arguments***

21. Applicant's arguments filed September 25, 2002 have been fully considered but are not found persuasive. It is noted for the record that applicant's arguments in this response are directed at the previously examined claims 15-19 (from the first Office Action on the merits). These claims have since been amended and are now withdrawn from consideration (see paragraphs 2-8 above). As newly added claims 42-56 are deemed to read on the previously examined invention, they are examined in this action and the arguments are addressed in as much as they pertain to rejection of these claims. The examiner's rationale is set forth below.

22. Applicants arguments on pages 9-10 are mainly directed to the limitation of "wherein said common ligand competes for cofactor binding" which the examiner has deemed to be a different invention than the one previously examined. However, the examiner maintains the position that the definitions in the specification for the terms discussed in the rejection are *very broad* and *open-ended*. As stated in the rejection, no limitations on the specific structure of the identified "bi-target ligand" are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention.

For example, the “common ligand” and “second/third ligands” must bind to their respective sites and the sites must be able to be determined. Most importantly, *the instant specification fails to identify that structure which is required for the claimed activity.*

23. Applicant argues that one would be able to predict how to determine each of the sites, find the appropriate ligands thereto and then put all of these pieces together to form the instant “bi-target ligand” as required by the method of the instant claims based on the specification’s teachings. The examiner respectfully disagrees. As stated in the rejection, this is a very unpredictable area of the art. The “predictability or lack thereof” in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.

24. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. See *In re Fisher*, 57 CCPA 1099,427 F.2d 833,839,166 USPQ 18,24(1970). Additionally, the Board has held on the issue of unpredictability that “... the unpredictability of an art area alone may be enough to create

a reasonable doubt as to the accuracy of statements in the specification.” *Ex parte Singh*, 17 U.S.P.Q.2d 1714, 1716 (B.P.A.I. 1990). In the absence of proper guidance (which the examiner deems is lacking in the instant case), a practitioner of the art of combinatorial chemistry would have to resort to a substantial amount of experimental trial and error to identify any “bi-target ligands” by the claimed method that have the required functional limitations. This trial and error would clearly constitute undue experimentation.

25. Applicant points out that examples are not required (Response, page 10, bottom). While it is true that an example is not required, it is often necessary to provide description and enablement for broad claims. Thus, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38USPQ 189, 191 (CCPA 1938). Also see MPEP 2164.02.

26. Applicant also argues that the “specification further teaches that methods such as NMR can be applied to identify sites of a common ligand proximal to a specificity site” and other methodology for orientation and linking of ligands (Response, page 11). However, this bears little correlation to the steps of the instantly claimed method and the portions of the specification referred to are prophetic and general in nature. Again, the specification does not specifically describe how to make and use any “bi-target ligands” that are identified or any specific “method for identifying a bi-target ligand”.

27. Also, see MPEP 716.09: Once the examiner has established a prima facie case of lack of enablement, the burden falls on the applicant to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would have been able to make and use the claimed invention using the disclosure as a guide. *In re Brandstadter*, 484 F.2d 1395, 179 USPQ 286 (CCPA 1973). Evidence to supplement a specification which on its face appears deficient under 35 U.S.C. 112 must establish that the information which must be read into the specification to make it complete would have been known to those of ordinary skill in the art. *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981).

28. Thus, for these reasons, the above rejection under 35 U.S.C. 112, first paragraph is maintained.

***Status of Claims/Conclusion***

29. No claims are allowed.

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the

advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

32. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.  
May 16, 2003



MAURIE GARCIA BAKER PH.D.  
PRIMARY EXAMINER